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(54) Title: CONTROL OF ARTHROPODS IN ANIMALS

(57) Abstract

A method of controlling parasites in or on an animal comprising administering to the animal a parasiticidally effective, substantially non-emetic 1-arylpyrazole.

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Control of Arthropods in Animals

The present invention relates to a method of control of parasites in animals, compositions comprising a compound effective for the said control and new compounds effective against parasites.

It is generally a goal of agronomists and veterinarians to possess sufficient means to control pests, particularly arthropods, when they attempt to invade or attack mammals, particularly domestic animals and/ or livestock. A classical method of controlling such pests has been the use of topical and/or systemic pesticides on or in the domestic animal which is being attacked. Generally effective treatments include the oral administration of insect growth regulators, such as lufenuron, or antihelminth compounds such as an ivermectin or an avermectin, or the topical application of the insecticide fipronil. It is advantageous to apply pesticides to animals in oral form so as to prevent the possible contamination of humans or the surrounding environment.

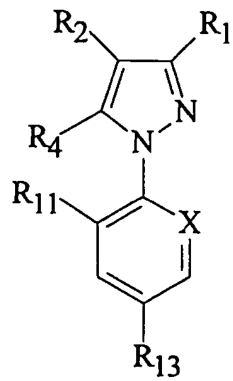
It is an object of the present invention to provide new pesticides which may be used in domestic animals.

Another object of the invention is to provide safer pesticides for domestic animals.

Another object of the invention is to provide new pesticides for domestic animals that may be used in lower doses than existing pesticides.

These objects are met in whole or in part by the present invention.

The present invention provides a method of controlling parasites in or on an animal comprising administering orally to the animal a parasiticidally effective, substantially non-emetic amount of a 1-arylpyrazole of formula (I):



(I)

wherein:

R_1 is cyano, acetyl, $C(S)NH_2$, alkyl, haloalkyl, $C(=NOH)NH_2$ or $C(=NNH_2)NH_2$;

R_2 is $S(O)_nR_3$; C_2-C_3 alkenyl, C_2-C_3 haloalkenyl, cycloalkyl, halocycloalkyl or C_2-C_3 alkynyl;

R_3 is alkyl or haloalkyl;

R_4 is $-N=C(R_5)-Z-R_6$, $-N=C(R_5)-N(R_7)-R_8$, or $-N(R_9)-C(R_5)=NR_6$;

R_5 is hydrogen; alkyl; or alkyl substituted by halogen, alkoxy, haloalkoxy or $-S(O)_mR_{15}$;

R_6 and R_7 each independently represent hydrogen, alkyl, C_3-C_5 alkenyl or C_3-C_5 alkynyl; or

alkyl substituted by one or more halogen, alkoxy, haloalkoxy, amino, alkylamino, dialkylamino, cyano or $-S(O)_mR_{15}$; or alkyl substituted by phenyl or pyridyl each of which is optionally substituted with one or more groups selected from halogen, nitro and alkyl; or

R_6 and R_7 may form together with the nitrogen to which they are attached a 3 to 7 membered ring which may additionally contain one or more heteroatoms selected from oxygen, nitrogen or sulfur;

R_8 is alkoxy, haloalkoxy, amino, alkylamino, dialkylamino, $R_{14}CO$- or $-S(O)_tR_{10}$;

R_9, R_{10} and R_{14} are alkyl or haloalkyl;

R_{11} and R_{12} are independently selected from halogen, hydrogen, CN and NO_2;

R_{13} is selected from halogen, haloalkyl, haloalkoxy, $-S(O)_qCF_3$, and $-SF_5$;

R_{15} is alkyl or haloalkyl;

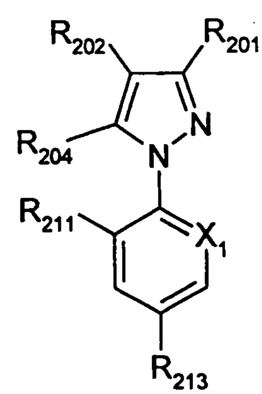
X is selected from nitrogen and C-R_{12};

Z is O, $S(O)_a$; or NR_7;

a, m, n and q are independently selected from 0, 1, and 2; and

t is 0 or 2; and veterinarily acceptable salts thereof.

In another aspect, the present invention provides a method of controlling parasites in or on an animal comprising administering orally to the animal a parasiticidally effective, substantially non-emetic amount of a 1-arylpyrazole of formula (XX):



(XX)

wherein:

R_{201} is cyano, C(O)alkyl, $C(S)NH_2$, alkyl, $C(=NOH)NH_2$ or $C(=NNH_2)NH_2$;

R_{202} is $S(O)_hR_{203}$, C_2-C_3 alkenyl, C_2-C_3 haloalkenyl, cycloalkyl, halocycloalkyl or C_2-C_3 alkynyl;

R_{203} is alkyl or haloalkyl;

R_{204} is $-N(R_{205})C(O)CR_{206}R_{207}R_{208}$, $-N(R_{205})C(O)$aryl, or $-N(R_{205})C(O)OR_{207}$;

R_{205} is alkyl, haloalkyl, cycloalkyl, halocycloalkyl, cycloalkylalkyl, halocycloalkylalkyl, alkoxyalkyl, haloalkoxyalkyl, C_3-C_5 alkenyl, C_3-C_5 haloalkenyl, C_3-C_5 alkynyl, C_3-C_5 haloalkynyl;

R_{206} is hydrogen, halogen, alkoxy, haloalkoxy, alkoxyalkyl, haloalkoxyalkyl, formyloxy, alkylcarbonyloxy, haloalkylcarbonyloxy, alkylthio, haloalkylthio, alkylsulfinyl, haloalkylsulfinyl, alkylsulfonyl, haloalkylsulfonyl, alkylamino, dialkylamino, haloalkylamino, di(haloalkyl)amino, cycloalkyloxy, halocycloalkyloxy, alkoxyalkoxy, haloalkoxyalkoxy, alkoxyalkoxyalkoxy, aryloxy, or arylalkoxy;

R_{207} and R_{208} are independently hydrogen, alkyl, haloalkyl, cycloalkyl, or halocycloalkyl; or R_{207} and R_{208} may form together with the carbon to which they are attached a 3 to 7 membered ring which additionally may contain one or more heteroatoms selected from nitrogen, oxygen and sulfur;

X_1 is selected from nitrogen and C-R_{212};

R_{211} and R_{212} are independently selected from halogen, hydrogen, CN and NO_2;

R_{213} is selected from halogen, haloalkyl, haloalkoxy, $-S(O)_kCF_3$, and $-SF_5$; and

h and k are independently selected from 0, 1, and 2;

and veterinarily acceptable salts thereof.

By the term "veterinarily acceptable salts" is meant salts the anions of which are known and accepted in the art for the formation of salts for veterinary use. Suitable acid addition salts, e.g. formed by

compounds of formulae (I) and (XX) containing a basic nitrogen atom, e.g. an amino group, include salts with inorganic acids, for example hydrochlorides, sulphates, phosphates and nitrates and salts with organic acids for example acetic acid.

Unless otherwise specified, alkyl and alkoxy groups are generally lower alkyl and alkoxy groups, that is having from one to six carbon atoms, preferably from one to four carbon atoms. Generally, the haloalkyl, haloalkoxy and alkylamino groups have from one to four carbon atoms. The haloalkyl and haloalkoxy groups can bear one or more halogen atoms; preferred groups of this type include $-CF_3$ and $-OCF_3$. Cycloalkyl groups generally have from 3 to 6 carbon atoms, preferably from 3 to 5 carbon atoms and may be substituted by one or more halogen atoms. . Alkenyl, haloalkenyl, alkynyl, and haloalkynyl groups generally contain from 3 to 5 carbon atoms. By the term aryl is generally meant phenyl, pyridyl, furyl, and thiopheneyl, each of which is optionally substituted by one or more halogen, alkyl, haloalkyl, nitro, alkoxy, haloalkoxy, hydroxy, amino, alkylamino or dialkylamino. In compounds of formula (I), by the term substituted alkyl is meant alkyl which is substituted by one or more halogen, alkoxy, haloalkoxy, amino, alkylamino, dialkylamino, cyano or $-S(O)_mR_{15}$; or alkyl substituted by phenyl or pyridyl each of which is optionally substituted with one or more groups selected from halogen, nitro and alkyl; wherein R_{15} is alkyl or haloalkyl and m is zero, one or two. Preferably in compounds of formula (I), alkyl groups are generally substituted by from one to five halogen atoms, preferably from one to three halogen atoms. Chlorine and fluorine atoms are preferred.

Compounds of formula (I) wherein R_4 is $-N=C(R_5)-Z-R_6$, Z is NR_7 and R_6 represents a hydrogen atom may exist as the tautomeric

double bond isomer form $-NH-C(R_5)=N-R_7$. It is to be understood that both such forms are embraced by the present invention.

In compounds of formula (XX) the following examples of radicals are provided:

An example of cycloalkylalkyl is cyclopropylmethyl;

an example of cycloalkoxy is cyclopropyloxy;

an example of alkoxyalkyl is CH_3OCH_2-;

an example of alkoxyalkoxy is CH_3OCH_2O-;

An example of alkoxyalkoxyalkoxy is $CH_3OCH_2OCH_2O$-;

An example of aryloxy is the phenoxy radical; and

An example of the arylalkoxy radical is benzyloxy or 2-phenylethoxy.

Generally, in dialkylamino or di(haloalkyl)amino radicals, the alkyl and haloalkyl groups on nitrogen may be chosen independently of one another.

It is also to be understood that enantiomeric and diastereomeric forms of the compounds of formulae (I) and (XX) and salts thereof are embraced by the present invention. Compounds of formula (I) may be generally prepared according to known processes, for example as described in European Patent Application 511845 or other processes according to the knowledge of a man skilled in the art of chemical synthesis.

By the term non-emetic is meant a compound that does not generally elicit emesis from the animal when a protective, preventative or cleaning dose is administered to the animal. By the term emesis is meant vomiting. Generally an emetic substance elicits the said emesis in less than 24 hours after administration, preferably less than 8 hours, more preferably less than 2 hours. Generally when the compounds of the invention are administered to a population of animals, more than

70% of the animals are free of emesis, preferably more than 80%, most preferably more than 90%.

A preferred class of compounds of formula (I) for use in the control of parasites in animals are those wherein:

R_1 is cyano or alkyl;

R_2 is $S(O)_nR_3$;

R_3 is alkyl or haloalkyl;

R_4 is $-N=C(R_5)-Z-R_6$;

R_5 is hydrogen, alkyl or haloalkyl;

Z is O, $S(O)_a$; or NR_7;

R_6 and R_7 are independently selected from hydrogen and unsubstituted or substituted alkyl; or

R_6 and R_7 may form together with the nitrogen to which they are attached a 3 to 7 membered ring which may additionally contain one or more heteroatoms selected from oxygen, nitrogen or sulfur;X is selected from nitrogen and $C-R_{12}$;

R_{11} and R_{12} are independently selected from halogen, hydrogen, CN and NO_2;

R_{13} is selected from halogen, haloalkyl, haloalkoxy, $-S(O)_qCF_3$, and $-SF_5$;

a, n and q are independently selected from 0, 1, and 2.

3) Preferably R_6 is alkyl which is substituted by one or more halogen, alkoxy, haloalkoxy, amino, alkylamino, dialkylamino, sulfide, sulfoxide, sulfone, or phenyl or pyridyl moieties of which each phenyl or pyridyl moiety is optionally substituted with one or more groups selected from halo, nitro, and alkyl.

Preferably the method of the invention has one or more of the following features:

R_1 is cyano;

R_4 is -N=C(R_5)-Z-R_6 and Z is -NR_7;

X is C-R_{12}; R_{11} and R_{12} represent a chlorine atom; and R_{13} is CF_3, OCF_3 or -SF_5;

R_{12} is -$S(O)_nCF_3$ and n is 0, 1, or 2.

A further preferred class of compounds of formula (I) for use in the control of parasites in animals are those wherein:

R_1 is cyano or alkyl; R_4 is -N=C(R_5)-Z-R_6; and R_5 is hydrogen or C_1-C_3 alkyl.

The compounds of formula (I) for use in the control of parasites in animals, preferably have one or more of the following features:

R_1 is cyano or methyl;

R_3 is halomethyl (preferably CF_3);

R_{11} and R_{12} each independently represent a halogen atom;

X is C-R_{12};

R_{13} is haloalkyl (preferably CF_3), haloalkoxy (preferably OCF_3), or -SF_5; or

n is 0, 1 or 2 (preferably 0 or 1).

A further preferred class of compounds of formula (I) for use in the control of parasites in animals are those wherein:

R_1 is cyano;

R_2 is $S(O)_nR_3$;

R_3 is halomethyl;

R_4 is -N=C(R_5)-Z-R_6;

Z is NR_7;

R_5 is hydrogen or alkyl;

R_6 and R_7 each independently represent hydrogen, alkyl, alkenyl or alkynyl; or alkyl substituted by one or more halogen, alkoxy, haloalkoxy, amino, alkylamino, dialkylamino, cyano or $-S(O)_mR_{15}$; or alkyl substituted by phenyl or pyridyl which rings are optionally substituted with one or more groups selected from halogen, nitro and alkyl;

X is selected from nitrogen and $C-R_{12}$;

R_{11} and R_{12} each independently represent a halogen atom;

R_{13} is selected from haloalkyl, haloalkoxy and $-SF_5$;

R_{15} is alkyl or haloalkyl; and

m and n are independently selected from 0, 1, and 2.

A further preferred class of compounds of formula (I) for use in the control of parasites in animals is that wherein:

R_1 is cyano;

R_2 is $S(O)_nCF_3$;

R_4 is $-N=C(R_5)-Z-R_6$ or $-N=C(R_5)-N(R_7)-R_8$;

Z is NR_7;

R_5 is hydrogen or alkyl;

R_6 and R_7 each independently represent hydrogen, alkyl, alkenyl or alkynyl; or alkyl substituted by one or more halogen, alkoxy, haloalkoxy, amino, alkylamino, dialkylamino, cyano or $-S(O)_mR_{15}$; or methyl substituted by phenyl or pyridyl which rings are optionally substituted with one or more groups selected from halogen, nitro and alkyl;

R_8 is alkoxy, haloalkoxy, amino, alkylamino, dialkylamino or $-S(O)_tR_{10}$;

X is selected from nitrogen and $C-R_{12}$;

R_{10} and R_{15} independently represent alkyl or haloalkyl;

R_{11} and R_{12} each represent a chlorine atom;

R_{13} is CF_3 or $-SF_5$; and

m and n are 0, 1 or 2; and t is 0 or 2.

A further preferred class of compounds of formula (I) for use in the control of parasites in animals are those wherein:

R_1 is cyano;

R_2 is $S(O)_nCF_3$;

R_4 is $-N=C(R_5)-Z-R_6$;

Z is NR_7;

R_5 is hydrogen or methyl;

R_6 and R_7 each independently represent hydrogen, alkyl, alkenyl or alkynyl; or alkyl substituted by one or more halogen, alkoxy, haloalkoxy, amino, alkylamino, dialkylamino, cyano or $-S(O)_mR_{15}$; or alkyl substituted by phenyl or pyridyl which rings are optionally substituted with one or more groups selected from halogen, nitro and alkyl;

X is $C-R_{12}$;

R_{11} and R_{12} each represent a chlorine atom;

R_{13} is CF_3 or $-SF_5$;

R_{15} is alkyl or haloalkyl;

m is zero, one or two; and

n is 0 or 1.

A further preferred class of compounds of formula (I) for use in the control of parasites in animals are those wherein:

R_1 is cyano;

R_2 is $S(O)_nCF_3$;

R_4 is $-N=C(R_5)-Z-R_6$;

Z is NR_7;

R_5 and R_7 each represent a hydrogen atom;

R_6 is alkyl or haloalkyl;

X is C-R_{12};

R_{11} and R_{12} each represent a chlorine atom;

R_{13} is CF_3 or $-SF_5$; and

n is 0.

Compounds of formula (XX) which are preferred according to the present invention are those wherein:

wherein:

R_{201} is cyano;

R_{202} is $S(O)_hR_{203}$;

R_{203} is alkyl or haloalkyl;

R_{204} is $-N(R_{205})C(O)CR_{206}R_{207}R_{208}$;

R_{205} is alkyl, haloalkyl, cycloalkyl, cycloalkylalkyl and halocycloalkylalkyl;

R_{206} is alkoxy, haloalkoxy, or hydrogen;

R_{207} and R_{208} are independently hydrogen, alkyl, or haloalkyl; or

R_{207} and R_{208} may form together with the carbon to which they are attached a 3 to 7 membered ring which additionally may contain one or more heteroatoms selected from nitrogen, oxygen and sulfur;

X_1 is selected from nitrogen and C-R_{212};

R_{211} and R_{212} are independently selected from halogen, hydrogen, CN and NO_2;

R_{213} is selected from halogen, haloalkyl, haloalkoxy, $-S(O)_kCF_3$, and $-SF_5$; and

h and k are independently selected from 0, 1, and 2.

A preferred group of compounds of formula (XX) is that wherein the ring which is formed by R_{207} and R_{208} is interrupted by one or more heteroatoms, more preferably one oxygen atom.

The compounds of formula (I) of the present invention preferably have one or more of the following features:

R_{201} is cyano;

R_{203} is halomethyl, preferably CF_3;

R_{211} and R_{212} are independently halogen;

X_1 is C-R_{212};

R_{213} is haloalkyl, haloalkoxy or -SF_5; or

h is 0 or 1, or 2, preferably 0 or 1.

A preferred class of compounds that wherein R_{204} is $N(R_{205})C(O)CR_{206}R_{207}R_{208}$.

Another preferred class of compounds that wherein R_{204} is $N(R_{205})C(O)$aryl.

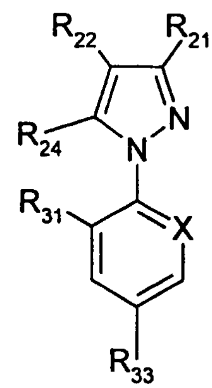
Another preferred class of compounds that wherein R_{204} is $N(R_{205})C(O)OR_{207}$.

Preferably R_{205} is C_1-C_4 alkyl, more preferably C_1-C_2 alkyl, most preferably methyl.

Preferably R_{206} is alkoxy, most preferably methoxy, ethoxy or propoxy.

Preferably R_{207} and R_{208} are both hydrogen.

Among the compounds which may be used in the invention some are new and hence in another aspect of the present invention there is provided a compoundof formula (II):



(II)

wherein:

R_{21} is cyano, alkyl, haloalkyl, , acetyl or -C(=S)NH_2, C(=NOH)NH_2 or C(=NNH_2)NH_2;

R_{22} is $S(O)_mR_{23}$;

R_{23} is alkyl or haloalkyl;

R_{24} is -N=C(R_{25})N(R_{26})(R_{27}) or -N=C(R_{25})-N(R_{27})-R_{28};

R_{25} represents hydrogen or alkyl; or alkyl substituted by one or more halogen, alkoxy, haloalkoxy or $-S(O)_mR_{35}$;

R_{26} and R_{27} each independently represent hydrogen, alkyl, alkenyl or alkynyl; or alkyl substituted by one or more halogen, alkoxy, haloalkoxy, amino, alkylamino, dialkylamino, cyano or $-S(O)_mR_{35}$; or alkyl substituted by phenyl or pyridyl which rings are optionally substituted with one or more groups selected from halogen, nitro and alkyl; wherein R_{35} is alkyl or haloalkyl and m is zero, one or two;

X is selected from nitrogen and C-R_{32};

R_{28} is alkoxy, haloalkoxy, amino, alkylamino, dialkylamino or $-S(O)_tR_{30}$;

R_{30} is alkyl or haloalkyl;

R_{31} and R_{32} are independently selected from halogen, hydrogen, CN and NO_2;

R_{33} is selected from halogen, haloalkyl, haloalkoxy, $-S(O)_rCF_3$, and $-SF_5$;

m and r are independently selected from 0, 1, and 2; and t is 0 or 2; with the exclusion of the compound wherein R_{21} is cyano; R_{22} is $-SCF_2CH_3$; R_{25} is hydrogen; X is C-R_{32}; R_{26} and R_{27} are methyl; R_{31} and R_{32} are chlorine; and R_{33} is trifluoromethyl; and veterinarily acceptable salts thereof.

A further class of novel compounds of formula (II) are those wherein:

R_{21} is cyano or methyl;

R_{22} is $S(O)_mR_{23}$;

R_{23} is haloalkyl;

R_{24} is $-N=C(R_{25})N(R_{26})(R_{27})$;

R_{25} and R_{27} are hydrogen or unsubstituted or substituted alkyl;

R_{26} is haloalkyl;

X is selected from nitrogen and C-R_{32};

R_{31} and R_{32} are independently selected from halogen, hydrogen, CN and NO_2;

R_{33} is selected from halogen, haloalkyl, haloalkoxy, $-S(O)_rCF_3$, and $-SF_5$;

m and r are independently selected from 0, 1, and 2; with the exclusion of the compound wherein R_{21} is cyano; R_{22} is $-SCF_2CH_3$; R_{25} is hydrogen; X is C-R_{32}; R_{26} and R_{27} are methyl; R_{31} and R_{32} are chlorine; and R_{33} is trifluoromethyl.

A preferred class of novel compounds of formula (II) are those wherein:

R_{21} is cyano;

R_{22} is $S(O)_mR_{23}$;

R_{23} is halomethyl;

R_{24} is -N=C(R_{25})N(R_{26})(R_{27});

R_{25} is hydrogen or alkyl;

R_{26} and R_{27} each independently represent hydrogen, alkyl, alkenyl or alkynyl; or alkyl substituted by one or more halogen, alkoxy, haloalkoxy, amino, alkylamino, dialkylamino, cyano or -S(O)$_m$R$_{15}$; or alkyl substituted by phenyl or pyridyl each of which is optionally substituted with one or more groups selected from halogen, nitro and alkyl; wherein R_{15} is alkyl or haloalkyl and m is zero, one or two;

X is selected from nitrogen and C-R_{32};

R_{31} and R_{32} each represent a chlorine atom;

R_{33} is selected from haloalkyl, haloalkoxy and -SF_5;

m is selected from 0, 1, and 2.

A further preferred class of novel compounds of formula (II) are those wherein:

R_{21} is cyano;

R_{22} is S(O)$_m$CF$_3$;

R_{24} is -N=C(R_{25})N(R_{26})(R_{27}); or -N=C(R_{25})-N(R_{27})-R_{28};

R_{25} is hydrogen or methyl;

R_{26} and R_{27} each independently represent hydrogen, alkyl, alkenyl or alkynyl; or alkyl substituted by one or more halogen, alkoxy, haloalkoxy, amino, alkylamino, dialkylamino, cyano or -S(O)$_m$R$_{15}$; or methyl substituted by phenyl or pyridyl which rings are optionally substituted with one or more groups selected from halogen, nitro and alkyl; wherein R_{15} is alkyl or haloalkyl and m is zero, one or two;

R_{28} is alkoxy, haloalkoxy, amino, alkylamino, dialkylamino or -S(O)$_t$R$_{30}$;

X is selected from nitrogen and C-R_{32};

R_{30} is alkyl or haloalkyl;

R_{31} and R_{32} each represent a chlorine atom;

R_{33} is CF_3 or $-SF_5$; and

m is 0, 1 or 2; and t is 0 or 2.

A more preferred class of novel compounds of formula (II) are those wherein:

R_{21} is cyano;

R_{22} is $S(O)_mCF_3$;

R_{24} is $-N=C(R_{25})N(R_{26})(R_{27})$;

R_{25} and R_{27} each independently represent hydrogen or methyl;

R_{26} represents hydrogen, alkyl, alkenyl or alkynyl; or alkyl substituted by one or more halogen, alkoxy, haloalkoxy, amino, alkylamino, dialkylamino, cyano or $-S(O)_mR_{15}$; or methyl substituted by phenyl or pyridyl which rings are optionally substituted with one or more groups selected from halogen, nitro and alkyl; wherein R_{15} is alkyl or haloalkyl and m is zero, one or two;

X is selected from nitrogen and $C-R_{32}$;

R_{31} and R_{32} each represent a chlorine atom;

R_{33} is CF_3 or $-SF_5$; and

m is 0, 1 or 2.

An especially preferred class of novel compounds of formula (II) are those wherein:

R_{21} is cyano;

R_{22} is $S(O)_mCF_3$;

R_{24} is $-N=C(R_{25})N(R_{26})(R_{27})$;

R_{25} and R_{27} each represent a hydrogen atom;

R_{26} is alkyl or (preferably) haloalkyl;

X is $C-R_{32}$;

R_{31} and R_{32} each represent a chlorine atom;

R_{33} is CF_3 or $-SF_5$; and

m is 0.

In another aspect of the present invention there is provided an compound of formula (XX) or a salt thereof as hereinbefore defined, provided that the compound is not 3-cyano-1-(2,6-dichloro-4-trifluoromethylphenyl)-5-(N-ethoxycarbonyl-N-methyl)amino-4-trifluoromethylthiopyrazole.

Most preferably, the following compounds of formula (I) and (XX) are preferred according to the present invention as listed in Tables 1 to 13. The Compound Numbers are for identification purposes only. The following symbols are hereby defined: Me means methyl; Et means ethyl; n-Pr means n-propyl; i-Pr means isopropyl; n-Bu means n-Butyl, and n-Pent means n-Pentyl; Cy means cyclopropyl.

Table 1

Compounds of formula (I) wherein R_1 is cyano; R_2 is SCF_3; R_{11} is Cl, X is C-Cl, R_4 is $-N=C(R_5)ZR_6$, Z is NR_7, R7 is H, and R_{13} is CF_3 or SF_5.

Compound Number $R_{13}=CF_3$	Compound Number $R_{13}=SF_5$	R_5	R_6
201-1	201-2	Me	Me
202-1	202-2	Me	Et
203-1	203-2	Me	n-Pr
204-1	204-2	Me	i-Pr
205-1	205-2	Me	n-Bu
206-1	206-2	H	H

207-1	207-2	H	Et
208-1	208-2	H	n-Pr
209-1	209-2	H	i-Pr
210-1	210-2	H	n-Bu
211-1	211-2	H	CH_2CF_3
212-1	212-2	H	$(CH_2)_2CF_3$
213-1	213-2	H	CH_2OMe
214-1	214-2	H	$(CH_2)_2OCF_3$
215-1	215-2	Me	CH_2CF_3
216-1	216-2	Me	$(CH_2)_2CF_3$
217-1	217-2	Me	$(CH_2)_2OMe$
218-1	218-2	Me	$(CH_2)_2NMe_2$

Table 2

Compounds of formula (I) wherein R_1 is cyano; R_{11} is Cl; R_4 is -N=C(R_5)ZR_6 and Z is NR7.

Cmpd No.	R2	R5	R6	R7	X	R13
219	SCF3	H	CH3	CH3	C-Cl	CF3
220	SO2CF3	H	CH3	CH3	C-Cl	CF3
221	SCF3	H	CH2CN	H	C-Cl	CF3
222	SCF3	H	CH3	H	C-Cl	CF3
223	SOCF3	H	CH2Ph	H	C-Cl	CF3
224	SCF3	H	CH2Ph	H	C-Cl	CF3
225	SOCF3	H	CH3	H	C-Cl	CF3
226	SOCF3	H	CH3	H	C-Cl	CF3
227	SOCF3	H	CH2CF3	H	C-Cl	CF3
228	SO2CF3	H	2-propynyl	H	C-Cl	CF3
229	SO2CF3	H	CH2Ph	H	C-Cl	CF3
230	SO2CF3	H	CH2CF3	H	C-Cl	CF3
231	SOCF3	H	CH3	CH3	C-Cl	CF3
232	SCF3	H	CH2CF3	H	C-Cl	CF3
233	SCF3	H	CH2CF3	H	C-Cl	CF3
234	SCF3	H	2-propenyl	H	C-Cl	CF3
235	SCF3	H	2-propynyl	H	C-Cl	CF3

236	SOCF3	H	2-propynyl	H	C-Cl	CF3
237	SCF3	H	CH2OEt	H	N	CF3
238	SCF3	H	CH2OCH2CF3	CH3	C-Cl	CF3
239	SO2CF3	H	CH2CF3	CH3	C-Cl	SF5
240	SCF3	H	CH2CF3	H	N	SF5
241	SOCF3	H	CH2CH2CF3	H	C-Cl	CF3
242	SO2CF3	H	(CH2)3CF3	H	C-Cl	CF3
243	SCF3	H	(CH2)2N(CH3)2	H	C-Cl	CF3
244	SO2CF3	CH3	CH2(4-Cl Ph)	H	C-Cl	CF3
245	SCF3	H	CH2SO2CF3	H	C-Cl	CF3
246	SCF3	H	CH2(4-pyridyl)	H	C-Cl	CF3
247	SCF3	H	CH2(3-NO2 Ph)	H	C-Cl	CF3
248	SCF3	H	CH2CH2SCH3	H	C-Cl	CF3
249	SOCF3	H	CH2CF3	CH3	C-Cl	CF3

Note: Compound number 232 is the acetate salt, and compound number 233 is the citrate salt.

Table 3

Compounds of formula (I) wherein R_1 is cyano; R_{11} is Cl; and R_4 is -N=C(R_5)-N(R_7)-R_8.

Cmpd No.	R2	R5	R8	R7	X	R13
250	SCF3	H	OEt	H	C-Cl	CF3
251	SCF3	H	NHCH3	H	C-Cl	CF3
252	SCF3	H	NHCH3	CH3	C-Cl	CF3
253	SCF3	H	OCH2CF3	H	C-Cl	CF3
254	SCF3	H	N(CH3)2	H	N	SF5
255	SCF3	H	NH2	H	C-Cl	CF3
256	SCF3	H	S-nPr	H	C-Cl	CF3
257	SO2CF3	Et	S-nPr	H	C-Cl	SF5
258	SCF3	H	SO2CH3	H	C-Cl	CF3

The following compounds of formula (XX) are preferred according to the present invention as listed in Tables 4-12.

<u>Table 4</u>

Compounds of formula (XX) wherein R_{201} is cyano; R_{202} is SCF_3; R_{204} is $N(R_{205})C(O)CR_{206}R_{207}R_{208}$; R_{207} and R_{208} =H; R_{211} is Cl, X_1 is C-Cl, and $R_{213}$is CF_3 or SF_5.

Compound Number (R_{213}= CF_3)	Compound Number (R_{213}=SF_5)	R_{205}	R_{206}
1-1	1-2	Me	H
2-1	2-2	Me	OMe
3-1	3-2	Me	OEt
4-1	4-2	Me	O-i-Pr
5-1	5-2	Me	O-n-Bu
6-1	6-2	Et	H
7-1	7-2	Et	OMe
8-1	8-2	Et	OEt
9-1	9-2	Et	O-i-Pr
10-1	10-2	Et	O-n-Bu
11-1	11-2	n-Pr	H
12-1	12-2	n-Pr	OMe
13-1	13-2	n-Pr	OEt
14-1	14-2	n-Pr	O-i-Pr
15-1	15-2	n-Pr	O-n-Bu
16-1	16-2	i-Pr	H
17-1	17-2	i-Pr	OMe
18-1	18-2	i-Pr	OEt
19-1	19-2	i-Pr	O-i-Pr
20-1	20-2	i-Pr	O-n-Bu
21-1	21-2	n-Bu	H
22-1	22-2	n-Bu	OMe
23-1	23-2	n-Bu	OEt
24-1	24-2	n-Bu	O-i-Pr
25-1	25-2	n-Bu	O-n-Bu
26-1	26-2	CH_2Cy	H
27-1	27-2	CH_2Cy	OMe
28-1	28-2	CH_2Cy	OEt

29-1	29-2	CH_2Cy	O-i-Pr
30-1	30-2	CH_2Cy	O-n-Bu
31-1	31-2	CH_2CCH	H
32-1	32-2	CH_2CCH	OMe
33-1	33-2	CH_2CCH	OEt
34-1	34-2	CH_2CCH	O-i-Pr
35-1	35-2	CH_2CCH	O-n-Bu
36-1	36-2	Me	OAc
37-1	37-2	Me	CH_2OMe
38-1	38-2	Me	CH_2OEt
39-1	39-2	Me	O-i-Pr
40-1	40-2	Me	O-n-Bu
41-1	41-2	Me	OCH_2CF_3

Table 5

Compounds of formula (XX) wherein R_{201} is cyano; R_{202} is $S(O)CF_3$; R_{204} is $N(R_{205})C(O)CR_{206}R_{207}R_{208}$; R_{207} and R_{208} =H; R_{211} is Cl, X_1 is C-Cl, and R_{213} is CF_3 or SF_5.

Compound Number (R_{213}= CF_3)	Compound Number (R_{213}=SF_5)	R_{205}	R_{206}
1-3	1-4	Me	H
2-3	2-4	Me	OMe
3-3	3-4	Me	OEt
4-3	4-4	Me	O-i-Pr
5-3	5-4	Me	O-n-Bu
6-3	6-4	Et	H
7-3	7-4	Et	OMe
8-3	8-4	Et	OEt
9-3	9-4	Et	O-i-Pr
10-3	10-4	Et	O-n-Bu

11-3	11-4	n-Pr	H
12-3	12-4	n-Pr	OMe
13-3	13-4	n-Pr	OEt
14-3	14-4	n-Pr	O-i-Pr
15-3	15-4	n-Pr	O-n-Bu
16-3	16-4	i-Pr	H
17-3	17-4	i-Pr	OMe
18-3	18-4	i-Pr	OEt
19-3	19-4	i-Pr	O-i-Pr
20-3	20-4	i-Pr	O-n-Bu
21-3	21-4	n-Bu	H
22-3	22-4	n-Bu	OMe
23-3	23-4	n-Bu	OEt
24-3	24-4	n-Bu	O-i-Pr
25-3	25-4	n-Bu	O-n-Bu
26-3	26-4	CH_2Cy	H
27-3	27-4	CH_2Cy	OMe
28-3	28-4	CH_2Cy	OEt
29-3	29-4	CH_2Cy	O-i-Pr
30-3	30-4	CH_2Cy	O-n-Bu
31-3	31-4	CH_2CCH	H
32-3	32-4	CH_2CCH	OMe
33-3	33-4	CH_2CCH	OEt
34-3	34-4	CH_2CCH	O-i-Pr
35-3	35-4	CH_2CCH	O-n-Bu
36-3	36-4	Me	OAc
37-3	37-4	Me	CH_2OMe
38-3	38-4	Me	CH_2OEt
39-3	39-4	Me	O-i-Pr
40-3	40-4	Me	O-n-Bu
41-3	41-4	Me	OCH_2CF_3

Compound 3-3 was separated into its enantiomers R3-3 and S3-3

Table 6

Compounds of formula (XX) wherein R_{201} is cyano; R_{202} is $S(O)_2CF_3$; R_{204} is $N(R_{205})C(O)CR_{206}R_{207}R_{208}$; R_{207} and R_{208} = H; R_{211} is Cl, X_1 is C-Cl, and R_{213} is CF_3 or SF_5.

Compound Number (R_{213}= CF_3)	Compound Number (R_{213}=SF_5)	R_{205}	R_{206}
1-5	1-6	Me	H
2-5	2-6	Me	OMe
3-5	3-6	Me	OEt
4-5	4-6	Me	O-i-Pr
5-5	5-6	Me	O-n-Bu
6-5	6-6	Et	H
7-5	7-6	Et	OMe
8-5	8-6	Et	OEt
9-5	9-6	Et	O-i-Pr
10-5	10-6	Et	O-n-Bu
11-5	11-6	n-Pr	H
12-5	12-6	n-Pr	OMe
13-5	13-6	n-Pr	OEt
14-5	14-6	n-Pr	O-i-Pr
15-5	15-6	n-Pr	O-n-Bu
16-5	16-6	i-Pr	H
17-5	17-6	i-Pr	OMe
18-5	18-6	i-Pr	OEt
19-5	19-6	i-Pr	O-i-Pr
20-5	20-6	i-Pr	O-n-Bu
21-5	21-6	n-Bu	H
22-5	22-6	n-Bu	OMe
23-5	23-6	n-Bu	OEt
24-5	24-6	n-Bu	O-i-Pr
25-5	25-6	n-Bu	O-n-Bu
26-5	26-6	CH_2Cy	H
27-5	27-6	CH_2Cy	OMe

28-5	28-6	CH_2Cy	OEt
29-5	29-6	CH_2Cy	O-i-Pr
30-5	30-6	CH_2Cy	O-n-Bu
31-5	31-6	CH_2CCH	H
32-5	32-6	CH_2CCH	OMe
33-5	33-6	CH_2CCH	OEt
34-5	34-6	CH_2CCH	O-i-Pr
35-5	35-6	CH_2CCH	O-n-Bu
36-5	36-6	Me	OAc
37-5	37-6	Me	CH_2OMe
38-5	38-6	Me	CH_2OEt
39-5	39-6	Me	O-i-Pr
40-5	40-6	Me	O-n-Bu
41-5	41-6	Me	OCH_2CF_3

Table 7

Compounds of formula (XX) wherein R_{201} is cyano; R_{202} is SCF_3; R_{204} is $N(R_{205})C(O)CR_{206}R_{207}R_{208}$; R_{211} is Cl; X_1 is C-Cl; and R_{213} is CF_3 or SF_5-

Compound Number (R_{213}= CF_3)	Compound Number (R_{213}=SF_5)	R_{205}	R_{206}	R_{207}, R_{208}
1-7	1-8	Me	H	$-CH_2CH_2CH_2O-$
2-7	2-8	Et	H	$-CH_2CH_2CH_2O-$
3-7	3-8	i-Pr	H	$-CH_2CH_2CH_2O-$
4-7	4-8	Pr	H	$-CH_2CH_2CH_2O-$
5-7	5-8	Bu	H	$-CH_2CH_2CH_2O-$
6-7	6-8	Cy	H	$-CH_2CH_2CH_2O-$
7-7	7-8	CH_2Cy	H	$-CH_2CH_2CH_2O-$

Compound 1-7 was also separated into its enantiomers, called (R)1-7 and (S)1-7.

Table 8

Compounds of formula (XX) wherein R_{201} is cyano; R_{202} is $S(O)CF_3$; R_{204} is $N(R_{205})C(O)CR_{206}R_{207}R_{208}$; R_{211} is Cl, X_1 is C-Cl; and R_{213} is CF_3 or SF_5.

Compound Number (R_{213}= CF_3)	Compound Number (R_{213}=SF_5)	R_{205}	R_{206}	R_{207}, R_{208}
1-9	1-10	Me	H	$-CH_2CH_2CH_2O-$
2-9	2-10	Et	H	$-CH_2CH_2CH_2O-$
3-9	3-10	i-Pr	H	$-CH_2CH_2CH_2O-$
4-9	4-10	Pr	H	$-CH_2CH_2CH_2O-$
5-9	5-10	Bu	H	$-CH_2CH_2CH_2O-$
6-9	6-10	CH_2Cy	H	$-CH_2CH_2CH_2O-$
7-9	7-10	Cy	H	$-CH_2CH_2CH_2O-$

Compound 1-9 was separated into its diastereomers, (R,R)1-9, (S,R)1-9, (S,S)1-9, (R,S)1-9. The first designation of absolute configuration refers to the configuration of the sulfoxide moiety, the second to the chiral carbon.

Table 9

Compounds of formula (XX) wherein R_{201} is cyano; R_{202} is $S(O)_2CF_3$; R_{204} is $N(R_{205})C(O)CR_{206}R_{207}R_{208}$; R_{211} is Cl; X_1 is C-Cl; and R_{213} is CF_3 or SF_5-

Compound Number (R_{213}= CF_3)	Compound Number (R_{213}=SF_5)	R_{205}	R_{206}	R_{207}, R_{208}
1-11	1-12A	Me	H	$-CH_2CH_2CH_2O-$
2-11	2-12A	Et	H	$-CH_2CH_2CH_2O-$
3-11	3-12A	i-Pr	H	$-CH_2CH_2CH_2O-$
4-11	4-12A	Pr	H	$-CH_2CH_2CH_2O-$
5-11	5-12A	Bu	H	$-CH_2CH_2CH_2O-$
6-11	6-12A	Cy	H	$-CH_2CH_2CH_2O-$
7-11	7-12A	CH_2Cy	H	$-CH_2CH_2CH_2O-$

Compound 1-11 was also separated into its diastereomers, (R)1-11 and (S)1-11 .

Table 10

Compounds of formula (XX) wherein R_{201} is cyano; R_{204} is $N(R_{205})C(O)CR_{206}R_{207}R_{208}$; R_{207} and R_{208} are H; R_{211} is Cl, X_1 is C-Cl; and R_{213} is CF_3 or SF_5.

Compound Number (R_{213}= CF_3)	Compound Number (R_{213}=SF_5)	R_{205}	R_{206}
R_{202}=SCF_3			
1-12	1-13	Cy	H
2-12	2-13	Cy	OMe
3-12	3-13	Cy	OEt
4-12	4-13	Cy	i-O-Pr
5-12	5-13	Cy	O-n-Bu
R_{202}=$S(O)CF_3$			
6-12	6-13	Cy	H
7-12	7-13	Cy	OMe
8-12	8-13	Cy	OEt
9-12	9-13	Cy	O-i-Pr
10-12	10-13	Cy	O-n-Bu
R_{202}=$S(O)_2CF_3$			
11-12	11-13	Cy	H
12-12	12-13	Cy	OMe
13-12	13-13	Cy	OEt
14-12	14-13	Cy	O-i-Pr
15-12	15-13	Cy	O-n-Bu

Table 11

Compounds of formula (XX) wherein R_{201} is cyano; R_{204} is

$-N(R_{205})C(O)OR_{207}$; R_{211} is Cl; X_1 is C-Cl, and R_{213} is CF_3 or SF_5.

Compound Number (R_{213}= CF_3)	Compound Number (R_{213}=SF_5)	R_{205}	R_{207}
R_{202} is SCF_3			
67-1	67-2	Me	Me
68-1	68-2	Me	Et
69-1	69-2	Me	i-Pr
70-1	70-2	Me	n-Pr
71-1	71-2	Et	Me
72-1	72-2	Et	Et
73-1	73-2	Et	i-Pr
74-1	74-2	Et	n-Pr
75-1	75-2	n-Pr	Me
76-1	76-2	n-Pr	Et
77-1	77-2	n-Pr	i-Pr
78-1	78-2	n-Pr	n-Pr
79-1	79-2	i-Pr	Me
80-1	80-2	i-Pr	Et
81-1	81-2	i-Pr	i-Pr
82-1	82-2	i-Pr	n-Pr
R_{202} is $S(O)CF_3$			
83-1	83-2	Me	Me
84-1	84-2	Me	Et
85-1	85-2	Me	i-Pr
86-1	86-2	Me	n-Pr
87-1	87-2	Et	Me
88-1	88-2	Et	Et
89-1	89-2	Et	i-Pr
90-1	90-2	Et	n-Pr
91-1	91-2	n-Pr	Me
92-1	92-2	n-Pr	Et
93-1	93-2	n-Pr	i-Pr

94-1	94-2	n-Pr	n-Pr
95-1	95-2	i-Pr	Me
96-1	96-2	i-Pr	Et
97-1	97-2	i-Pr	i-Pr
98-1	98-2	i-Pr	n-Pr
R_{202} is $S(O)_2CF_3$			
99-1	99-2	Me	Me
100-1	100-2	Me	Et
101-1	101-2	Me	i-Pr
102-1	102-2	Me	n-Pr
103-1	103-2	Et	Me
104-1	104-2	Et	Et
105-1	105-2	Et	i-Pr
106-1	106-2	Et	n-Pr
107-1	107-2	n-Pr	Me
108-1	108-2	n-Pr	Et
109-1	109-2	n-Pr	i-Pr
110-1	110-2	n-Pr	n-Pr
111-1	111-2	i-Pr	Me
112-1	112-2	i-Pr	Et
113-1	113-2	i-Pr	i-Pr
114-1	114-2	i-Pr	n-Pr

Table 12

Compounds of formula (XX) wherein R_{201} is cyano; R_{202} is $S(O)_hCF_3$; R_{204} is $N(R_{205})C(O)CR_{206}R_{207}R_{208}$; R_{211} is Cl; X_1 is C-Cl, and R_{213} is CF_3 or SF_5.

Compound Number (R_{213}= CF_3)	Compound Number (R_{213}=SF_5)	h	R_{205}	R_{206}	R_{207}	R_{208}
115-1	115-2	0	Me	H	Me	Me
116-1	116-2	0	Me	OEt	H	Me
117-1	117-2	0	Me	H	cyclopropyl	
118-1	118-2	0	Me	OMe	H	Me

119-1	119-2	0	Me	OEt	Me	Me
120-1	120-2	2	Me	OCH_2CH_2OMe	H	H
121-1	121-2	0	Me	H	$-CH_2CH_2CH_2CH_2O-$	
122-1	122-2	1	Me	OEt	H	Me
123-1	123-2	0	Me	H	H	Me
124-1	124-2	0	Me	H	H	Et

Table 13

Compounds of formula (XX) wherein R_{201} is cyano; R_{202} is $S(O)_hCF_3$; R_{204} is $N(R_{205})C(O)$aryl; R_{211} is Cl; X_1 is C-Cl, R_{205} is CH_3; and R_{213} is CF_3 or SF_5. Within this table the following symbols are defined:

Ph means phenyl; Fu means furyl

Th means the thiophene radical

Pyr means pyridyl

Compound Number (R_{213}= CF_3)	Compound Number (R_{213}=SF_5)	aryl
R_{202} is SCF_3		
125-1	125-2	Ph
126-1	126-2	4-OMe-Ph
127-1	127-2	4-CF_3-Ph
128-1	128-2	2-Th
129-1	129-2	3-Th
130-1	130-2	2-Fu
131-1	131-2	3-Fu
132-1	132-2	2-Pyr
133-1	133-2	3-Pyr
134-1	134-2	4-Pyr
135-1	135-2	6-Cl-2-Pyr
136-1	136-2	6-CF_3-2-Pyr
137-1	137-2	5-Cl-2-Fu
138-1	138-2	5-CF_3-2-Fu
139-1	139-2	5-OMe-2-Th
140-1	140-2	5-CF_3-2-Th

R_{202} is $S(O)CF_3$		
125-3	125-4	Ph
126-3	126-4	4-OMe-Ph
127-3	127-4	4-CF_3-Ph
128-3	128-4	2-Th
129-3	129-4	3-Th
130-3	130-4	2-Fu
131-3	131-4	3-Fu
132-3	132-4	2-Pyr
133-3	133-4	3-Pyr
134-3	134-4	4-Pyr
135-3	135-4	6-Cl-2-Pyr
136-3	136-4	6-CF_3-2-Pyr
137-3	137-4	5-Cl-2-Fu
138-3	138-4	5-CF_3-2-Fu
139-3	139-4	5-OMe-2-Th
140-3	140-4	5-CF_3-2-Th
R_{202} is $S(O)_2CF_3$		
125-5	125-6	Ph
126-5	126-6	4-OMe-Ph
127-5	127-6	4-CF_3-Ph
128-5	128-6	2-Th
129-5	129-6	3-Th
130-5	130-6	2-Fu
131-5	131-6	3-Fu
132-5	132-6	2-Pyr
133-5	133-6	3-Pyr
134-5	134-6	4-Pyr
135-5	135-6	6-Cl-2-Pyr
136-5	136-6	6-CF_3-2-Pyr
137-5	137-6	5-Cl-2-Fu
138-5	138-6	5-CF_3-2-Fu
139-5	139-6	5-OMe-2-Th
140-5	140-6	5-CF_3-2-Th

The present invention also relates to a composition comprising a parasiticidally effective, substantially non-emetic amount of a compound of formula (I) or a salt thereof or a compound of formula (XX) or a salt thereof and an acceptable carrier. Acceptable carriers for the use of the compounds are generally known to the skilled addressee concerned with pest control in animals, particularly domestic animals, most preferably dogs or cats.

The compositions which can be used in the invention can comprise generally from about 0.001 to 95% of the compound of formula (I) or a salt thereof or a compound of formula (XX) or a salt thereof. The remainder of the composition up to 100% comprises a carrier as well as generally various additives. In this specification and the accompanying claims, percentages are by weight.

The diluted liquid formulations generally comprise from about 0.001 to about 3% of compound of formula (I) or a salt thereof or a compound of formula (XX) or a salt thereof, preferably from about 0.1 to about 0.5%.

Solid formulations generally comprise from about 0.1 to about 8% of compound of formula (I) or a salt thereof or a compound of formula (XX) or a salt thereof ,preferably from about 0.5 to about 1.5%.

Compositions for oral administration comprise one or more of the compounds of general formula (I) or salts thereof or compounds of formula (XX) or salts thereof in association with veterinarily acceptable carriers or coatings and include, for example, tablets, pills, capsules, gels, drenches, medicated feeds, medicated drinking water, medicated dietary supplements, slow-release boluses or other slow-release devices intended to be retained within the gastro-intestinal tract. Any of these may incorporate the active ingredients contained within micro-capsules or coated with acid-labile or alkali-labile or other pharmaceutically acceptable enteric coatings. Feed premixes or concentrates containing

compounds of the present invention for use in preparation of medicated diets, drinking water or other materials for consumption by animals may also be used. In a highly preferred embodiment, the compositions are administered postprandially, preferably from just after a meal to 2 hours after the meal.

In a highly preferred embodiment, there is provided a product which is readily chewed by the animal and which product does generally not allow human contamination when the product is provided to the animal by hand.

The compounds of general formula (I) or salts thereof or compounds of formula (XX) or salts thereof may be administered before, during or after meals The compounds of general formula (I) or salts thereof or compounds of formula (XX) or salts thereof may be mixed with a carrier and/or a foodstuff.

According to the present invention the compound of formula (I) or a salt thereof or a compound of formula (XX) or a salt thereof is administered orally in a dose to the animal in a dose range generally from 0.1 to 500 mg/kg of the compound of formula (I) or a salt thereof or a compound of formula (XX) or a salt thereof per kilogram of animal body weight (mg/kg), preferably from 1 to 100 mg/kg, more preferably from 1 to 50 mg/kg, even more preferably from 2 to 25 mg/kg, most preferably from 3 to 15 mg/kg

According to the present invention, the frequency of treatment of the animal, preferably the domestic animal to be treated by the compound of formula (I) or a salt thereof or a compound of formula (XX) or a salt thereof is generally from about once per week to about once per year, preferably from about once every two weeks to about once every six months, more preferably from about once every two weeks to once every three months, and most preferably from about once every two weeks to about once every six weeks.

Generally the animal to be treated is a domestic animal, preferably a domestic companion animal. More preferably the animal to be treated is a dog and/or a cat.

The compounds of the invention may be administered most advantageously with another parasiticidally effective material, such as an endoparasiticide, and/or an ectoparasiticide, and/or an endectoparasiticide. For example, such compounds include macrocyclic lactones such as avermectins or milbemycins e.g., ivermectin; pyratel (generally adminsitered as pyrantel pamoate) or an insect growth regulator such as lufenuron or methoprene.

By the term "parasites" as used in the specification and claims is meant endoparasites and ectoparasites of warm-blooded animals, particularly ectoparasites. Preferably, fleas and/or ticks are controlled by the method of the present invention.

Illustrative of specific parasites of various host animals which may be controlled by the method of this invention include arthropods such as:

Mites: Mesostigmata spp. e.g. mesostigmatids such as the chicken mite, Dermanyssus gallinae; itch or scab mites such as Sarcoptidae spp. for example Sarcoptes scabiei; mange mites such as Psoroptidae spp. including Chorioptes bovis and Psoroptes ovis; chiggers e.g. Trombiculidae spp. for example the north american chigger, Trombicula alfreddugesi;

Ticks: e.g., soft-bodied ticks including Argasidae spp. for example Argas spp. and Ornithodoros spp ; hard-bodied ticks including Ixodidae spp., for example Rhipicephalus sanguineus, and Boophilus spp.;

Lice: sucking lice, e.g., Menopon spp. and Bovicola spp.; biting lice, e.g., Haematopinus spp., Linognathus spp. and Solenopotes spp.;

Fleas: e.g., Ctenocephalides spp., such as dog flea (Ctenocephalides canis) and cat flea (Ctenocephalides felis); Xenopsylla

spp. such as oriental rat flea [Xenopsylla cheopis]; and Pulex spp. such as human flea [Pulex irritans];

True bugs: e.g., Cimicidae or including the common bed bug (Cimex lectularius);, Triatominae spp. including triatomid bugs also known as kissing bugs; for example Rhodnius prolixus and Triatoma spp.;

bloodsucking adult flies: (e.g., horn fly [Haematobia irritans], horse fly [Tabanus spp.], stable fly [Stomoxys calcitrans], black fly [Simulium spp.], deer fly [Chrysops spp.], louse fly [Melophagus ovinus], tsetse fly [Glossina spp.], mosquitoes [Culex spp., Anopheles spp., and Aedes spp.); and

parasitic fly maggots: (e.g., bot fly [Oestrus ovis and Cuterebra spp.], blow fly [Phaenicia spp.], screwworm [Cochliomyia hominivorax], cattle grub [Hypoderma spp.], fleeceworm.

The present invention also relates to a use of a compound of formula (I) or a salt thereof or a compound of formula (XX) or a salt thereof hereinbefore described as a therapeutic agent, preferably for animals, more preferably for domestic animals.

The veterinary composition may be sterile or non-sterile. It may be a liquid (e.g. aqueous) or solid (e.g., dry) composition, in particular a freeze-dried composition, which, by addition of water or another liquid, orally effective solutions may be prepared.

The present invention also relates to a use of a compound of formula (I) or a salt thereof or a compound of formula (XX) or a salt thereof as hereinbefore defined for the manufacture of a veterinary composition for the control of parasites in or on an animal.

The present invention also relates to a method of cleaning animals in good health comprising the application to the animal of a

compound of formula (I) or a salt thereof or a compound of formula (XX) or a salt thereof as hereinbefore defined to the animal.

The method of cleaning an animal is not a method of treatment by therapy of the animal body per se, because

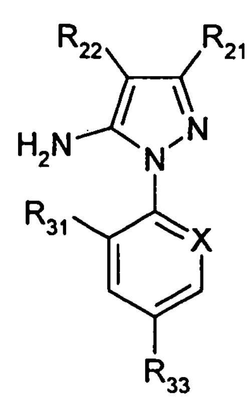
(a) the animal is in good health and requires no substantial treatment to correct a deficiency of health;

(b) the cleaning of the animal is not intended to be done by veterinary personnel, but by persons interested in the cleaning of the animal; and

(c) the purpose of such cleaning is to avoid unpleasant conditions for humans and the environment in which humans inhabit so as to not infest the said humans with arthropods carried by the animal.

By "carrier" is meant an organic or inorganic material, which can be natural or synthetic, and which is associated with the compound and which facilitates its application to the animal. This carrier is thus generally inert and should be arthropocidally acceptable. The carrier can be solid (e.g., clay, silicates, silica, resins, wax.) or liquid (e.g., water, alcohols, ketones, oil solvents, polar aprotic solvents) An example of an oil solvent is corn oil. An example of a polar aprotic solvent is dimethyl sulfoxide.

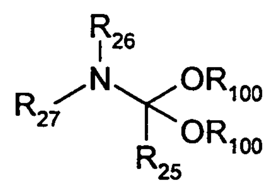
INCORPORERThe compounds of formula (II) wherein R_{21}, R_{22}, R_{24}, R_{31}, R_{33} and X are as defined above may be prepared from the compounds of formula (III):



(III)

wherein R_{21}, R_{22}, R_{31}, R_{33} and X are as defined above, using processes described in European Patent Publications 0511845 or 0659745.

According to a feature of the present invention, compounds of formula (II) wherein R_{21}, R_{22}, R_{31}, R_{33} and X are as defined above and R_{24} is $-N{=}C(R_{25})-NR_{26}R_{27}$ wherein R_{25}, R_{26} and R_{27} are as defined above may be prepared by reacting a compound of formula (III) with a compound of formula (IV):

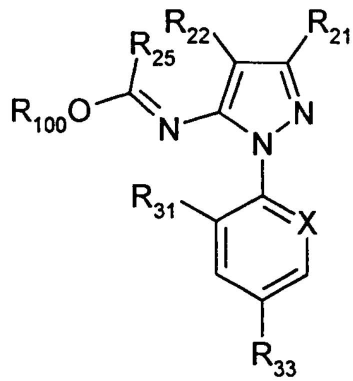


(IV)

wherein R_{25}, R_{26} and R_{27} are as defined above and R_{100} is generally an alkyl group. The reaction is optionally conducted in the presence of a catalyst such as a mineral or organic acid (for example hydrochloric acid), generally using from 1 to 100 equivalents of (IV), preferably using 1 to 10 equivalents of (IV), and is preferably conducted in an organic solvent such as tetrahydrofuran, toluene, or N,N-dimethylformamide, at a temperature of from 0°C to 150°C. Additional adjuvants such as drying agents (e.g. magnesium sulfate, potassium carbonate, or molecular sieves) may also be advantageous to the reaction. Compounds of formula (IV) are known or may be prepared by known procedures.

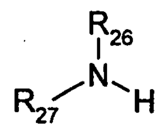
According to a feature of the present invention, compounds of formula (II) wherein R_{21}, R_{22}, R_{31}, R_{33} and X are as defined above and R_{24} is $-N{=}C(R_{25})-NR_{26}R_{27}$ wherein R_{25}, R_{26} and R_{27} are as

defined above, may be prepared by the reaction of a compound of formula (V):



(V)

wherein R_{21}, R_{22}, R_{25}, R_{31}, R_{33}, X and R_{100} are as defined above, with a compound of formula (VI):



(VI)

wherein R_{26} and R_{27} are as defined above. The reaction is generally conducted using the same conditions as used for the preparation of compounds of formula (II) by the reaction of compounds of formula (III) with compounds of formula (IV).

According to a feature of the present invention, compounds of formula (II) wherein R_{24} is -N=C(R_{25})-N$R_{27}R_{28}$, and R_{21}, R_{22}, R_{25}, R_{27}, R_{31}, R_{33} and X are as defined above, and R_{28} is COR_{34} wherein R_{34} is as defined above, may be prepared by the reaction of the corresponding compounds of formula (II) wherein R_{24} is -N=C(R_{25})-NR_{27}H with an acid chloride of formula (VII):

R_{34}COCl (VII)

wherein R_{34} is as defined above. The reaction is generally performed in the presence of a base such as a trialkylamine for example

triethylamine in a solvent such as dichloromethane, at a temperature of from 0°C to 50°C.

According to a feature of the present invention, compounds of formula (II) wherein R_{24} is -N=C(R_{25})-N$R_{27}R_{28}$, and R_{21}, R_{22}, R_{25}, R_{27}, R_{31}, R_{33} and X are as defined above and R_{28} is -S(O)$_t$$R_{30}$ may be prepared by the reaction of the corresponding compound of formula (II) wherein R_{24} is -N=C(R_{25})-NR_{27}H with a sulfonyl chloride or a sulfenyl chloride of formula (VIII):

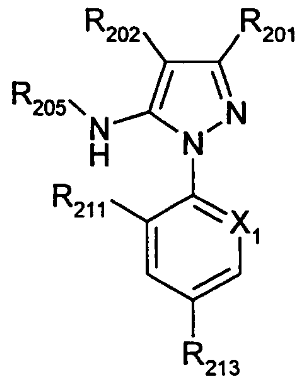
$$R_{30}S(O)_tCl \quad \text{(VIII)}$$

The reaction is generally performed in the presence of a weak base such as a trialkylamine for example triethylamine, or pyridine in a solvent such as dichloromethane, at a temperature of from 0°C to 50°C.

Compounds of formula (VI), (VII) and (VIII) are known or may be prepared by known procedures.

Compounds of formula (III) and (V) may be generally prepared according to known processes, for example as described in International Patent Publications WO 87/3781, WO 93/6089, WO 94/21606 WO 97/07102, WO 98/24767, , WO 98/28277, WO 98/28278 and WO 98/28279,, European Patent Application 295117, 846686, and United States Patent 5232940..

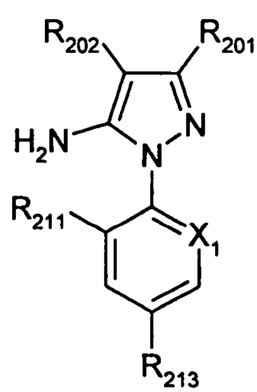
In another aspect of the present invention, compounds of formula (XX) wherein R_{204} is -N(R_{205})C(O)C$R_{206}R_{207}R_{208}$, N(R_{205})C(O)aryl, or N(R_{205})C(O)OR_{207} are generally prepared from compounds of formula (XXI):



(XXI)

respectively by reaction with halides of formulae $X_2C(O)CR_{206}R_{207}R_{208}$, $X_2C(O)$aryl, or $X_2C(O)OR_{207}$, wherein R_{201}, R_{202}, R_{205}, R_{206}, R_{207}, R_{208}, R_{211}, R_{213}, and X_1 are defined above and wherein X_2 is a halogen atom. The reaction is generally carried ouT in the presence of a base, generally using from 1 to 10 molar equivalents of the halide, and is preferably conducted in the presence of an organic solvent such as tetrahydrofuran, methylene chloride, at a temperature of from 0°C to 150°C.

Compounds of formula (XXI) may be prepared from a compound of formula (XXII):



(XXII)

by reaction with a compound of formula (XXIII):

$$X_2R_{205}(XXIII)$$

wherein R201, R202, R205, R211, R213, X1 and X2 are defined above. Compounds of formula (XXIII) are generally known in the art as alkylhalides or substituted alkylhalides. Compounds of formula XXII may be prepared by methods described in International Patent Publications WO 87/3781, WO 93/6089, WO 94/21606, WO 97/07102, WO 98/24767, , WO 98/28277, WO 98/28278 and WO 98/28279, European Patent Application 295117, 659745, 846686, and United States Patent 5232940 or other methods known to the person skilled in the art.

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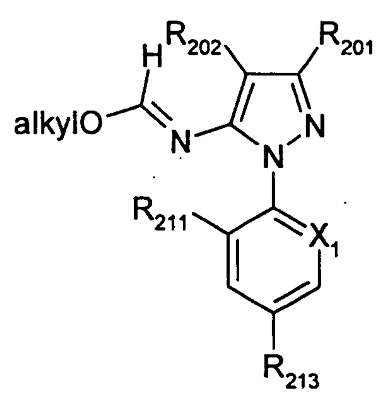
Alternatively compounds of formula (XXI) may be prepared by reduction of compounds of formula (XXIV):



(XXIV)

wherein R_{201}, R_{202}, R_{211}, R_{213} and X_1 are defined above. The reduction generally is effected by the use of a standard hydride ion donor, for example sodium borohydride or sodium cyanoborohydride. The reaction is generally effected in an polar solvent such as ethanol or

methanol and generally using from 1 to 10 molar equivalents of the hydride, and is preferably conducted at temperature of from -100°C to 150°C.

Compounds of formula (XXIV) may be prepared using methods described in EP 295117, WO 97/22593 or other methods known to those skilled in the art.

In another aspect of the invention there are provided the compounds 3-Cyano-1-(2,6-dichloro-4-trifluoromethylphenyl)-5-ethoxymethylideneamino-4-trifluoromethylsulfinylpyrazole and 3-cyano-1-(2,6-dichloro-4-trifluoromethylphenyl)-5-methylamino-4-trifluoromethylsulfinylpyrazole which are useful intermediates for the preparation of compounds for use according to the present invention.

Biological Example

Compounds 1-1, 2-1, 3-1, 4-1, 11-1, 13-1, 28-1, 31-1, 32-1, 36-1, 37-1, 38-1, 1-3, 2-3, 3-3, 4-3, 6-3, 41-3, 1-5, 2-5, 3-5, 6-5, 11-5, 27-5, 28-5, 1-7, 3-7, 5-7, 1-9, 1-11, 6-11, 7-11, 1-12, 11-12, 13-12, 67-1, 68-1, 69-1, 70-1, 72-1, 75-1, 76-1, 77-1, 78-1, 79-1, 80-1, 81-1, 82-1, 115-1, 116-1, 117-1, 118-1, 119-1, 120-1, 121-1, 122-1, 123-1, 124-1, 211-1, 219, 220, 221, 222, 223, 224, 225, 226, 227, 228, 229, 230, 231, 232, 233, R3-3, S3-3, R1-7, S1-7, (R,S)1-9, (R,R)1-9, (S,R)1-9, (S,S) 1-9, S1-11, R1-11, 126-1, 127-1 and 130-1 were formulated as a 30 mg/mL formulations in a 1:1 volume/volume solution of dimethyl sulfoxide and corn oil. Using this formulation, mixed breed dogs and cats were treated at a rate of 10 mg of the compound per kg (mg/kg)of body weight of the dog and 20 mg/kg of the cat treated. The animals were fasted for at least 8 hours prior to treatment, fed half of the daily ration

immediately prior to treatment, then allowed access to the remainder of the daily ration immediately following treatment.

All dogs were infested with cat fleas (Ctenocephalides felis) and with ticks (Rhipicephalus sanguineus) 1 day prior to administration of the compound. Cats were only infested with fleas. The initial flea and tick counts were performed 1 day after the administration of the compounds. At 7, 14, 21 and 28 days after treatment the dogs were re-infested with ticks and 8, 15, 22 and 29 days after treatment the dogs and cats were re-infested with fleas. At 1, 9, 16, 23 and 30 days after treatment the control of fleas and ticks in treated dogs and cats was determined versus a group of infested dogs and cats which received a placebo consisting of a 1:1 volume/volume solution of dimethyl sulfoxide and corn oil. To determine the efficacies of the compounds, the arthropods were combed from the animals and counted.

In the animals treated with the compounds above, there was substantially no emesis after 2, 8 and 24 hours. Generally long-term control of fleas and ticks was provided in dogs. In the cats treated, there was commercially acceptable control of fleas for at least one day post treatment.

The results of this example were superior to those obtained with compounds of the prior art, for example, fipronil.

The following non-limiting Synthesis Examples illustrate the preparation of compounds of formula (I) and the Reference Examples illustrate the preparation of intermediates used in their synthesis.

Synthesis Example 1

A solution of 5-amino-3-cyano-1-(2,6-dichloro-4-trifluoromethylphenyl)-4-trifluoromethylthiopyrazole (1 g) in N,N-dimethylformamide dimethyl acetal was heated at 50°C for 1 hour.

Evaporation of solvents gave 3-cyano-1-(2,6-dichloro-4-trifluoromethylphenyl)-5-N'-dimethylaminomethylideneamino-4-trifluoromethylthiopyrazole m.p.141°C.

By proceeding in a similar manner the following compounds were also prepared:

3-cyano-1-(2,6-dichloro-4-trifluoromethylphenyl)-5-N'-dimethylaminomethylideneamino-4-trifluoromethylsulfonylpyrazole m.p.209°C; and

3-cyano-1-(2,6-dichloro-4-trifluoromethylphenyl)-5-N'-dimethylaminomethylideneamino-4-trifluoromethylsulfinylpyrazole m.p.207°C.

Synthesis Example 2

A solution of 3-cyano-1-(2,6-dichloro-4-trifluoromethylphenyl)-5-ethoxymethylideneamino-4-trifluoromethylthiopyrazole (5 g) in ethanol was treated with benzylamine (11.4 ml), stirred overnight, evaporated and purified by reverse-phase column chromatography (C-18 stationary phase column, eluting with MeOH/water) to give 5-N'-benzylaminomethylideneamino-3-cyano-1-(2,6-dichloro-4-trifluoromethylphenyl)- 4-trifluoromethylthiopyrazole 1.18 g), m.p.113°C.

By proceeding in a similar manner the compounds of formula (II) wherein R_{21} is CN; R_{24} is -N=CH-NHR_{26}; R_{31} is Cl; X is C-Cl; and R_{33} is CF_3 shown in Table 4 were also prepared.

Table 4

Compd No.	R22	R26	M.P. °C
21	SCF3	CH2CN	175
211-1	SCF3	CH2CF3	130
222	SCF3	CH3	173
223	SOCF3	CH2Ph	173
225	SOCF3	CH3	144
226	SOCF3	CH3	144

227	SOCF3	CH2CF3	175
228	SO2CF3	2-propynyl	149
229	SO2CF3	CH2Ph	182
230	SO2CF3	CH2CF3	183
209-1	SCF3	iPr	
207-1	SCF3	CH2CH3	141

Reference Example 1

A solution of 5-amino-3-cyano-1-(2,6-dichloro-4-trifluoromethylphenyl)-4-trifluoromethylthiopyrazole (500 g) in triethyl orthoformate was treated with concentrated hydrochloric acid (10 ml) and heated at 50°C. After 8 hours the reaction mixture was evaporated to give a solid which was washed (heptane) and air-dried to give 3-cyano-1-(2,6-dichloro-4-trifluoromethylphenyl)-5-ethoxymethylideneamino-4-trifluoromethylthiopyrazole (217 g), m.p. 68°C.

By proceeding in a similar manner the following intermediates were also prepared:

3-cyano-1-(2,6-dichloro-4-trifluoromethylphenyl)-5-ethoxymethylideneamino-4-trifluoromethylsulfinylpyrazole, m.p.63°C; and 3-cyano-1-(2,6-dichloro-4-trifluoromethylphenyl)-5-ethoxymethylideneamino-4-trifluoromethylsulfonylpyrazole, m.p.118°C.

Synthesis Example 3

3-Cyano-1-(2,6-dichloro-4-trifluoromethylphenyl)-5-methylamino-4-trifluoromethylsulfinylpyrazole (111.55 g, 0.247 moles), triethylamine (62.45 g, 0.618 moles), 4-dimethylaminopyridine (3 g, 0.0247 moles), and tetrahydrofuran (700 ml) was combined. The resulting solution was heated to 45°C and ethoxyacetyl chloride (45.2 g,

0.37 mmol) was added dropwise over 10 min. After 1 h, the mixture was evaporated to a brown residue, which was dissolved in 500 ml of ethyl acetate and washed with 2 x 300 ml of water. The organic phase was dried over magnesium sulfate, filtered, and evaporated to a brown oil. The oil was triturated with 1 L of hot cyclohexane. The resulting solids were collected by filtration and washed with 500 ml of hot cyclohexane, then air dried to afford of compound 3-3 as a beige powder (116.7 g). Evaporation of the mother liquors afforded a second crop of compound 3-3 (8.4 g).

In a similar fashion or by modifications according to methods known to the skilled addressee, the following compounds were prepared. The compound numbers in the left column refer to the Tables cited above.

Compound Number	Mass Spectral molecular ion + 1 (M+1)
1-1	477
2-1	507
3-1	521
4-1	535
11-1	505
13-1	549
28-1	537
31-1	517
32-1	531
36-1	535
37-1	521
38-1	535
1-3	593
2-3	523

3-3	537
4-3	551
6-3	491
41-3	473
1-5	509
2-5	539
3-5	553
6-5	523
11-5	537
27-5	579
28-5	593
1-7	533
3-7	561
5-7	575
1-9	549
1-11	565
6-11	591
7-11	605
1-12	535
11-12	565
13-12	579
67-1	493
68-1	507
69-1	521
70-1	521
72-1	521
75-1	521
76-1	535
77-1	549

78-1	549
79-1	521
80-1	535
81-1	549
82-1	549
115-1	505
116-1	535
117-1	503
118-1	521
119-1	549
120-1	583
121-1	547
122-1	551
123-1	491
124-1	505
126-1	507
127-1	607
130-1	529

Reference Example 2:

Step A: Preparation of 3-Cyano-1-(2,6-dichloro-4-trifluoromethylphenyl)-5-ethoxymethylideneamino-4-trifluoromethylsulfinylpyrazole.

A 12-L three-necked flask fitted with an overhead stirrer, heating mantle, water separator (e.g. Dean Stark trap) with condenser was placed under a nitrogen atmosphere and charged with 1.475 kg (3.37 moles) of fipronil and 6 L of triethyl orthoformate. The suspension was

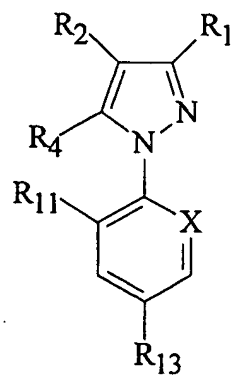
heated to reflux over 2.5 h, then at reflux for 3 h with collection and removal of the distillate. The mixture was cooled to room temperature, then evaporated under reduced pressure at a bath temperature of 60-80°C, then at 50°C overnight. The resulting beige solid, 1.717 kg (95.8 % by HPLC, 3.335 moles, 99% purity corrected yield) was used without further purification. (m.p. about 63°C)

Step B: Preparation of 3-Cyano-1-(2,6-dichloro-4-trifluoromethylphenyl)-5-methylamino-4-trifluoromethylsulfinylpyrazole.

A 50 L reactor was charged with 3-Cyano-1-(2,6-dichloro-4-trifluoromethylphenyl)-5-ethoxymethylideneamino-4-trifluoromethylsulfinylpyrazole (1.645 g, 3.335 moles) and absolute ethanol (16 L) under nitrogen. The solution was cooled to 10°C, and sodium borohydride (266 g, 7.03 moles) was added slowly such that the temperature, remained generally below 35°C. After 6.75 h, some additional sodium borohydride (25 g, 0.66 moles) was added and stirring was continued overnight. Acetic acid (1.3 L, 22.7 moles) was added to quench, followed by 16 L of water. The resulting precipitate was collected by filtration, washed with water, and air-dried. Recrystallization from methanol afforded 3-Cyano-1-(2,6-dichloro-4-trifluoromethylphenyl)-5-methylamino-4-trifluoromethylsulfinylpyrazole (350 g) as an off-white solid. (m.p. about 227°C)

CLAIMS

1. A method of controlling parasites in or on an animal comprising administering orally to the animal a parasiticidally effective, substantially non-emetic amount of a 1-arylpyrazole of formula (I):



(I)

wherein:

R_1 is cyano, acetyl, $C(S)NH_2$, alkyl, haloalkyl, $C(=NOH)NH_2$ or $C(=NNH_2)NH_2$;

R_2 is $S(O)_nR_3$; C_2-C_3 alkenyl, C_2-C_3 haloalkenyl, cycloalkyl, halocycloalkyl or C_2-C_3 alkynyl;

R_3 is alkyl or haloalkyl;

R_4 is $-N=C(R_5)-Z-R_6$, $-N=C(R_5)-N(R_7)-R_8$, or $-N(R_9)-C(R_5)=NR_6$;

R_5 is hydrogen; alkyl; or alkyl substituted by halogen, alkoxy, haloalkoxy or $-S(O)_mR_{15}$;

R_6 and R_7 each independently represent hydrogen, alkyl, C_3-C_5 alkenyl or C_3-C_5 alkynyl; or

alkyl substituted by one or more halogen, alkoxy, haloalkoxy, amino, alkylamino, dialkylamino, cyano or $-S(O)_mR_{15}$; or alkyl

substituted by phenyl or pyridyl each of which is optionally substituted with one or more groups selected from halogen, nitro and alkyl; or

R_6 and R_7 may form together with the nitrogen to which they are attached a 3 to 7 membered ring which may additionally contain one or more heteroatoms selected from oxygen, nitrogen or sulfur;

R_8 is alkoxy, haloalkoxy, amino, alkylamino, dialkylamino, $R_{14}CO$- or $-S(O)_tR_{10}$;

R_9, R_{10} and R_{14} are alkyl or haloalkyl;

R_{11} and R_{12} are independently selected from halogen, hydrogen, CN and NO_2;

R_{13} is selected from halogen, haloalkyl, haloalkoxy, $-S(O)_qCF_3$, and $-SF_5$;

R_{15} is alkyl or haloalkyl;

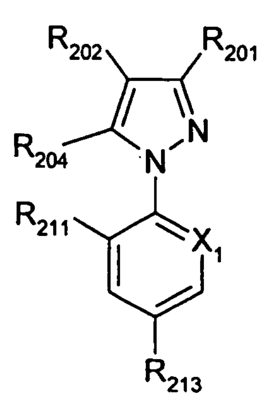
X is selected from nitrogen and C-R_{12};

Z is O, $S(O)_a$; or NR_7;

a, m, n and q are independently selected from 0, 1, and 2; and

t is 0 or 2; and veterinarily acceptable salts thereof.

2. A method of controlling parasites in or on an animal comprising administering orally to the animal a parasiticidally effective, substantially non-emetic amount of a 1-arylpyrazole of formula (XX):



(XX)

wherein:

R_{201} is cyano, C(O)alkyl, C(S)NH_2, alkyl, C(=NOH)NH_2 or C(=NH_2)NH_2;

R_{202} is $S(O)_hR_{203}$, C_2-C_3 alkenyl, C_2-C_3 haloalkenyl, cycloalkyl, halocycloalkyl or C_2-C_3 alkynyl;

R_{203} is alkyl or haloalkyl;

R_{204} is -N(R_{205})C(O)C$R_{206}R_{207}R_{208}$, –N(R_{205})C(O)aryl, or –N(R_{205})C(O)OR_{207};

R_{205} is alkyl, haloalkyl, cycloalkyl, halocycloalkyl, cycloalkylalkyl, halocycloalkylalkyl, alkoxyalkyl, haloalkoxyalkyl, C_3-C_5 alkenyl, C_3-C_5 haloalkenyl, C_3-C_5 alkynyl, C_3-C_5 haloalkynyl;

R_{206} is hydrogen, halogen, alkoxy, haloalkoxy, alkoxyalkyl, haloalkoxyalkyl, formyloxy, alkylcarbonyloxy, haloalkylcarbonyloxy, alkylthio, haloalkylthio, alkylsulfinyl, haloalkylsulfinyl, alkylsulfonyl, haloalkylsulfonyl, alkylamino, dialkylamino, haloalkylamino, di(haloalkyl)amino, cycloalkyloxy, halocycloalkyloxy, alkoxyalkoxy, haloalkoxyalkoxy, alkoxyalkoxyalkoxy, aryloxy, or arylalkoxy;

R_{207} and R_{208} are independently hydrogen, alkyl, haloalkyl, cycloalkyl, or halocycloalkyl; or R_{207} and R_{208} may form together with the carbon to which they are attached a 3 to 7 membered ring which additionally may contain one or more heteroatoms selected from nitrogen, oxygen and sulfur;

X_1 is selected from nitrogen and C-R_{212};

R_{211} and R_{212} are independently selected from halogen, hydrogen, CN and NO_2;

R_{213} is selected from halogen, haloalkyl, haloalkoxy, -$S(O)_kCF_3$, and -SF_5; and

h and k are independently selected from 0, 1, and 2;

and veterinarily acceptable salts thereof.

3. The method according to Claim 1 wherein the compound of formula (I) is that wherein:

R_1 is cyano or alkyl;

R_2 is $S(O)_nR_3$;

R_3 is alkyl or haloalkyl;

R_4 is $-N=C(R_5)-Z-R_6$;

R_5 is hydrogen, alkyl or haloalkyl;

Z is O, $S(O)_a$; or NR_7;

R_6 and R_7 are independently selected from hydrogen and unsubstituted or substituted alkyl; or

R_6 and R_7 may form together with the nitrogen to which they are attached a 3 to 7 membered ring which may additionally contain one or more heteroatoms selected from oxygen, nitrogen or sulfur;X is selected from nitrogen and $C-R_{12}$;

R_{11} and R_{12} are independently selected from halogen, hydrogen, CN and NO_2;

R_{13} is selected from halogen, haloalkyl, haloalkoxy, $-S(O)_qCF_3$, and $-SF_5$;

a, n and q are independently selected from 0, 1, and 2.

4. The method according to claim 2 wherein the compound of formula (XX) is that wherein:

R_{201} is cyano;

R_{202} is $S(O)_hR_{203}$;

R_{203} is alkyl or haloalkyl;

R_{204} is $-N(R_{205})C(O)CR_{206}R_{207}R_{208}$;

R_{205} is alkyl, haloalkyl, cycloalkyl, cycloalkylalkyl and halocycloalkylalkyl;

R_{206} is alkoxy, haloalkoxy, or hydrogen;

R_{207} and R_{208} are independently hydrogen, alkyl, or haloalkyl; or

R_{207} and R_{208} may form together with the carbon to which they are attached a 3 to 7 membered ring which additionally may contain one or more heteroatoms selected from nitrogen, oxygen and sulfur;

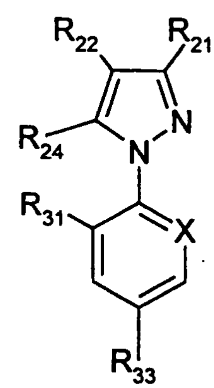
X_1 is selected from nitrogen and C-R_{212};

R_{211} and R_{212} are independently selected from halogen, hydrogen, CN and NO_2;

R_{213} is selected from halogen, haloalkyl, haloalkoxy, -$S(O)_kCF_3$, and -SF_5; and

h and k are independently selected from 0, 1, and 2.

5. A compound of formula (II):



(II)

wherein:

R_{21} is cyano, alkyl, haloalkyl, , acetyl or -$C(=S)NH_2$, $C(=NOH)NH_2$ or $C(=NNH_2)NH_2$;

R_{22} is $S(O)_mR_{23}$;

R_{23} is alkyl or haloalkyl;

R_{24} is $-N{=}C(R_{25})N(R_{26})(R_{27})$ or $-N{=}C(R_{25})\text{-}N(R_{27})\text{-}R_{28}$;

R_{25} represents hydrogen or alkyl; or alkyl substituted by one or more halogen, alkoxy, haloalkoxy or $-S(O)_mR_{35}$;

R_{26} and R_{27} each independently represent hydrogen, alkyl, alkenyl or alkynyl; or alkyl substituted by one or more halogen, alkoxy, haloalkoxy, amino, alkylamino, dialkylamino, cyano or $-S(O)_mR_{35}$; or alkyl substituted by phenyl or pyridyl which rings are optionally substituted with one or more groups selected from halogen, nitro and alkyl; wherein R_{35} is alkyl or haloalkyl and m is zero, one or two;

X is selected from nitrogen and $C\text{-}R_{32}$;

R_{28} is alkoxy, haloalkoxy, amino, alkylamino, dialkylamino or $-S(O)_tR_{30}$;

R_{30} is alkyl or haloalkyl;

R_{31} and R_{32} are independently selected from halogen, hydrogen, CN and NO_2;

R_{33} is selected from halogen, haloalkyl, haloalkoxy, $-S(O)_rCF_3$, and $-SF_5$;

m and r are independently selected from 0, 1, and 2; and t is 0 or 2; with the exclusion of the compound wherein R_{21} is cyano; R_{22} is $-SCF_2CH_3$; R_{25} is hydrogen; X is $C\text{-}R_{32}$; R_{26} and R_{27} are methyl; R_{31} and R_{32} are chlorine; and R_{33} is trifluoromethyl; and veterinarily acceptable salts thereof.

6. A compound of formula (XX) or a salt thereof as defined in Claim 2, provided that the compound is not 3-cyano-1-(2,6-dichloro-4-trifluoromethylphenyl)-5-(N-ethoxycarbonyl-N-methyl)amino-4-trifluoromethylthiopyrazole.

7. A composition comprising a parasiticidally effective, substantially non-emetic amount of a compound of formula (I) or a salt thereof as defined in Claim 1 or a compound of formula (XX) or a salt thereof as defined in Claim 2 and an acceptable carrier.

8. The method according to any one of Claims 1 to 4 wherein the animal is a domestic animal, preferably a dog or a cat.

9. The method according to any one of Claims 1, 2, 3, 4 or 8 wherein the 1-arylpyrazole is administered orally in a dose to the animal in a dose range generally from 0.1 to 500 mg/kg.

10. The method according to any one of Claims 1, 2, 3, 4, 8, or 9 wherein the 1-arylpyrazole is administered in a frequency of treatment from about once per week to about once per year.

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A. CLASSIFICATION OF SUBJECT MATTER
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According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 7 C07D A01N

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

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[X] Further documents are listed in the continuation of box C.

[X] Patent family members are listed in annex.

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X	EP 0 296 381 A (BAYER AG) 28 December 1988 (1988-12-28) page 6, line 5; claim 15	6
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